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Address to: Mail Stop: Amendment P.O. Box 1450 Alexandria, VA 22313-1450	Attorney Docket	GHDX-005
	Confirmation No.	5745
	First Named Inventor	Baker, Joffre B.
	Application Number	10/714,195
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	Group Art Unit	1634
	Examiner Name	SHAW, AMANDA MARIE
	Title	"Gene Expression Profiling of EGFR Positive Cancer"

DECLARATION OF STEVE SHAK, M.D. UNDER 37 C.F.R. §1.132

I, Steve Shak, M.D. declare as follows:

1. I am currently the Chief Medical Officer at Genomic Health, Inc., Redwood City, CA, 94063.
2. I joined Genomic Health, Inc. in 2000 as Chief Medical Officer. My scientific Curriculum Vitae, including my list of publications, is attached as Exhibit A.
3. During my employment with Genomic Health, I have been involved in supervising and analyzing gene expression profiling of EGFR positive colon cancer as described in Example 2 of the above-identified patent application.
4. I am also an inventor of the above-identified application.
5. I understand that some of the claims in the above-identified application have been rejected under 35 U.S.C. §112 as allegedly lacking enablement. I understand that the rejection is based, at least in part, on the assertion that the data in Example 2 of the specification cannot be interpreted in order to ascertain whether colon cancer patients with elevated levels of LAMC2 are actually less likely to respond to a treatment with each of the three claimed ErbB1 inhibitors because the specification and the prior Declaration of Joffre Baker, Ph.D. provide information regarding only

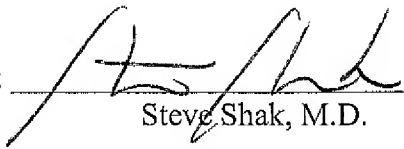
the combination of patients treated with EGFR inhibitors.

6. Thus, I understand that the Office has requested more information regarding the data, such as which drug each patient received and the expression level of LAMC2 for each patient.
7. Example 2 of the specification describes the study of 23 colon adenocarcinoma patients treated with an EGFR inhibitor using a 192 gene assay. mRNA was extracted from formalin-fixed colon tumor tissues obtained from each of the patients and molecular assays of quantitative gene expression on 192 genes were performed by RT-PCR. After removal of the colon tumor tissue, the patients were treated by or under the supervision of co-inventor Dr. Jose Baselga of Hospital Universitari Vall d'Hebron, Barcelona, Spain, with an EGFR inhibitor and the patients were determined to have a partial response, stable disease, or progressive disease. The level of expression of mRNA transcripts in the colon tumors from each of the 23 patients was then correlated with either the partial response of the patients or the clinical benefit to the patients. Table 3 in the specification is a result of an analysis of all 23 patient samples compared to the three patients within that group that showed a partial response. Table 3 indicates that overexpression of LAMC2 in colon tumor tissue showed a negative correlation with partial response to treatment with the EGFR inhibitors with a statistically significant p value of 0.0357.
8. Around early to mid November 2009, I inquired with Dr. Jose Baselga in order to obtain additional information regarding the EGFR inhibitors used in the study. I provided Irene Marimon, head of the Clinical Trials office at Vall d'Hebron and who initially generated the clinical benefit data of the 23 colon adenocarcinoma patients, with the patient identifier code that is specific for each of the 23 patients that were studied. Irene Marimon informed me in an email communication the anti-EGFR treatment each of the patients received. Upon information and belief, 15 patients were treated with the EGFR inhibitor EMD 72000 alone and 8 patients were

treated with cetuximab, with or without chemotherapy. I reviewed the patient data I received and determined that the three partial responders were treated with EMD 72000 alone.

9. I also prepared a graph showing the LAMC2 mRNA level that was used to prepare Table 3 in the specification for each of the 23 patients. *See* Exhibit B. I grouped the 23 patients into either non- partial responders ("No PR") or partial responders ("Yes PR"). Each circle represents a patient.
10. In my opinion, the attached graph in Exhibit B and Table 3 in the specification show that overexpression of LAMC2 in the colon tumor tissue is negatively correlated with partial response to treatment with an EGFR inhibitor. As stated in Table 3 of the specification, the correlation was statistically significant with a p value of 0.0357.
11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Date: 12/2/09

By: 
Steve Shak, M.D.